THE BRAIN METABOLIC-PERFUSION INDEX, A NEW SPECT OR PET METHOD TO DEFINE DEMENTIA PATHOPHYSIOLOGY FOR SELECTION AND MONITORING OF OPTIMAL THERAPY

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Abstract

Background: Cortical perfusion and metabolic indices (CPi, CMi) we and others used to analyze a single pathologic deficit do not afford optimal analysis in the majority of patients with mixed deficits.
Aim: Define an integrative brain metabolic-perfusion index (BMPi) to analyze the pathophysiologic spectrum of dementia and its response to therapy.

Methods: Labelled SPECT or PET tracers (Tc-99m-HMPAO, Tc-99m-ECD or F-18-FDG) were injected IV in a quiet dark room before or after flow stimulants, eg. 0.8 mg nitroglycerin sl. Ratios of metabolic and perfusion tracer activity within 60% to 30% isocontour defined CMi and CPi; white matter indices (WMi, WPi) used (30%-60%) to 30% isocontour rations. Brain perfusion or metabolic indices were: BPi=(CPi) (WPi)/b or BMi=(CMi) (WMi)/b where b=lateral ventricular background activity, as a fraction of peak brain activity, and BMPi=(BMi) (BPi)/(1-b).

Results: Ventricular background, b averages 0.2. Normal ranges for BPi 95-125%, BMi 100-125% and BMPi 120-200% can be calculated without WMi or WPi, since BPi=CPi (1-CPi)/b and BMi = CMi (1-CMi)/b.
Remarkably, BMPi represents overall potential for recovery, being maximal at CM i= CPi = 50%, near the CMi lower limit of normal (60+-10)% and decreasing more rapidly as CMi or CPi drop below normal. For CMi and CPi of 23%, BMPi is 98% and recovery potential is low; less marked deficits in CMi and/or CPi yield BMPi > 100%, with better prognosis for targeted therapy.

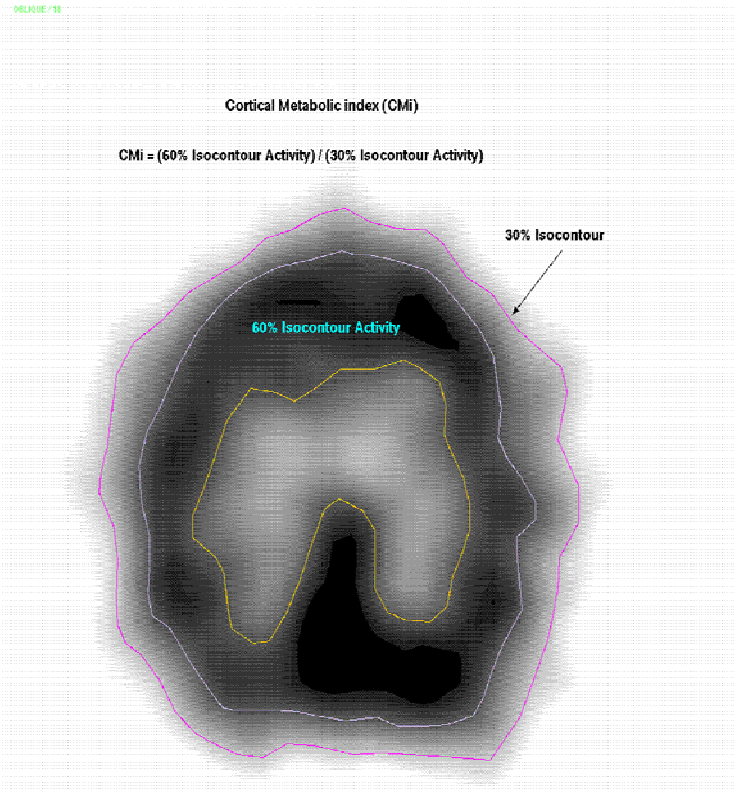
Conclusion: The BMPi for SPECT/PET integrates both neurodegenerative and vascular

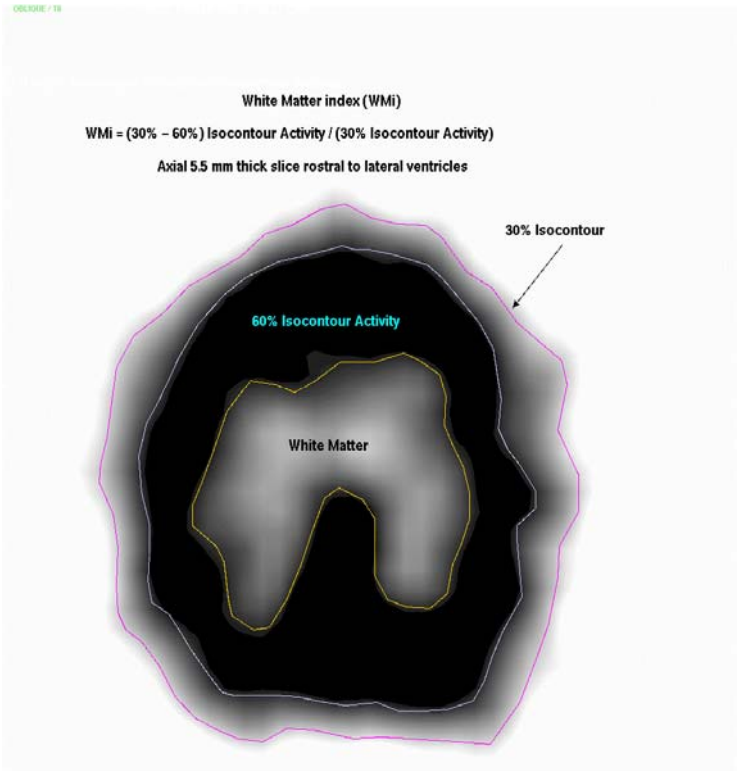
pathophysiologies in an analytic framework that provides a rational basis to select and monitor the entire spectrum of dementia therapies.

1. Cortical Metabolic indices were calculated from basal metabolic SPECT images using a metabolic tracer such as 200 MBq F-18 fluorodeoxy-glucose, 560 MBq Tc-99m-ECD or 500 MBq Tc-99m-HMPAO IV, given in a quiet dark room. The dual-head SPECT camera had 5.5 mm resolution using ultra-high resolution parallel-hole collimators, sensitivity 6500 cpm/MBq. Image matrix was 128 x 128 acquired in 64 frames/180 deg with 5 to 60 sec/frame (usually < 30 min per acquisition).

   Cortical Perfusion indices were similarly calculated using perfusion stimulants such as 0.8 mg nitroglycerin sublingual, 0.5 to 1.0 g acetazolamide IV, 10 g omega-3 unsaturated fish oil oral or 100 mg cilostazol oral and IV perfusion tracers such as Tc-99m-HMPAO or Tc-99m-ECD at suitable time intervals thereafter.
   Brain Metabolic indices were defined as: BMi = (CMi)(WMi) / b, where b is cerebral ventricular activity as a % of peak brain activity, typically near 20%, normalized by multiplying 20% by (20% / measured b), so that smaller measured b, corrected for scattering, (larger ventricles or more cerebral atrophy) leads to smaller BMi. Brain Perfusion indices were similarly calculated from perfusion-stimulated SPECT.
   The Brain Metabolic-Perfusion index BMPi was a cross product of its components, BMi and BPi, scaled by dividing by the normalizing factor (1-b), for which b was taken as the simple average of the normalized b values calculated as described above for the perfusion study and that calculated for the metabolic study. Again, larger ventricles (with lower b and greater cerebral atrophy) decrease BMPi.

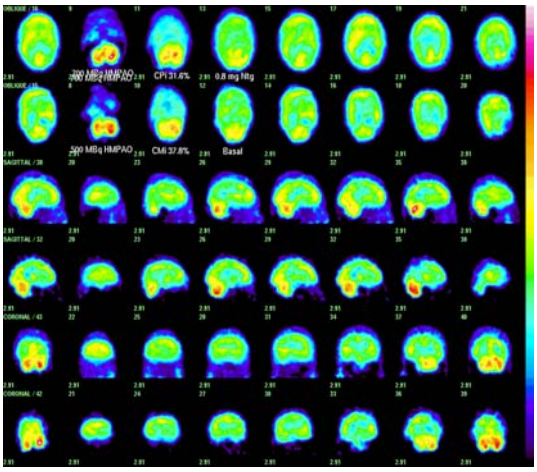
2.

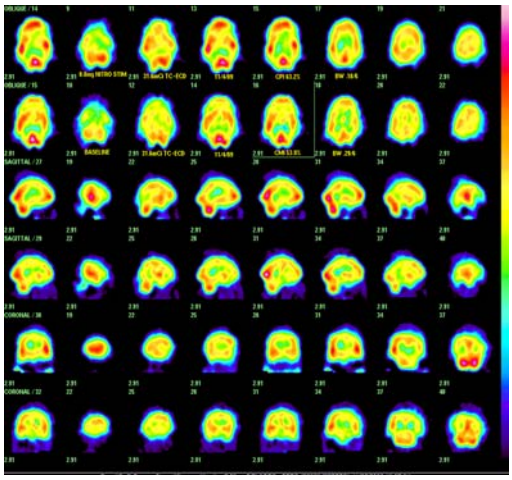

Cortical Metabolic index (CMi)
CMi = (60% Isocontour Activity) / (30% Isocontour Activity)
30% Isocontour
60% Isocontour Activity


White Matter index (WMi)
WMi = (30% – 60%) Isocontour Activity / (30% Isocontour Activity)
Axial 5.5 mm thick slice rostral to lateral ventricles
30% Isocontour
60% Isocontour Activity
White Matter

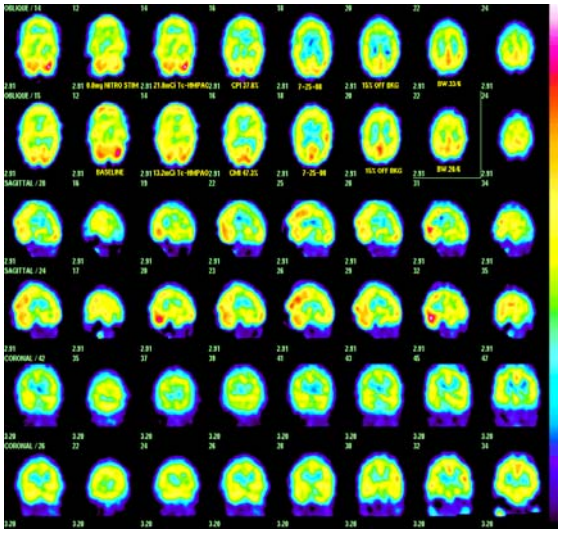
3. Below on the left is brain SPECT, perfusion-stimulated the top and basal the bottom of each 3 paired image rows, for a 43 y.o. alcoholic with mild Wernicke's, history of head trauma and long-term heavy cigarette smoking with CMi 37.8%, CPi 31.6%, BMi 173%; BPi 132%, BMPi 150%, BMPc 189% reflecting potential for improvement.

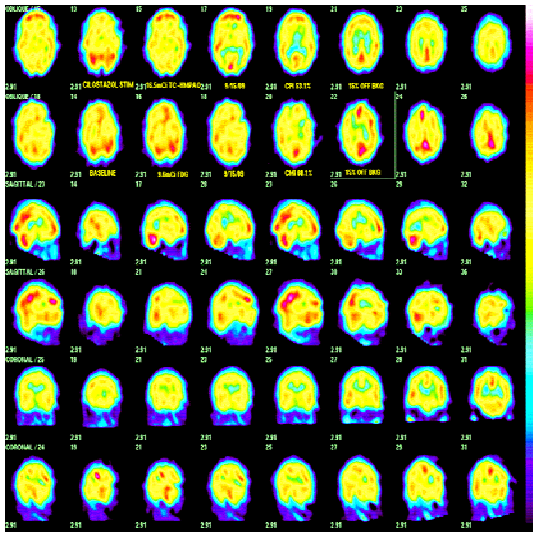
Below on the right is similarly displayed brain SPECT for a 62 year-old woman business owner with minor headaches and ideal BP control (124/72), hyperlipidemia (LDL 82, HDL 80, Trigl 76, Chol 177) mg/dl and type 2 diabetes mellitus (hgb A1c 5.5%) with CMi 53.9%, CPi 63.2%, BMi 156%, BPi 215%, BMPi 387%, BMPc 447%, demonstrating near maximal values.



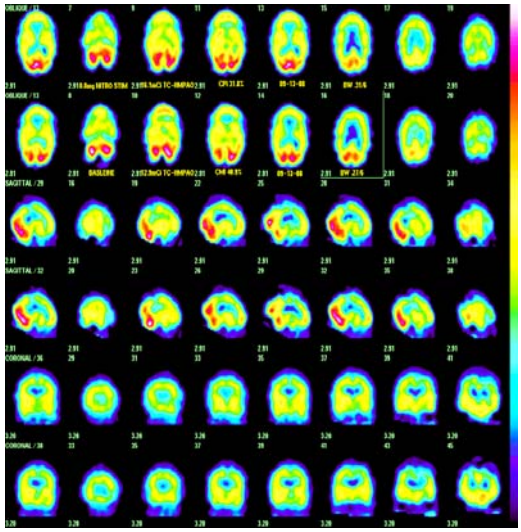


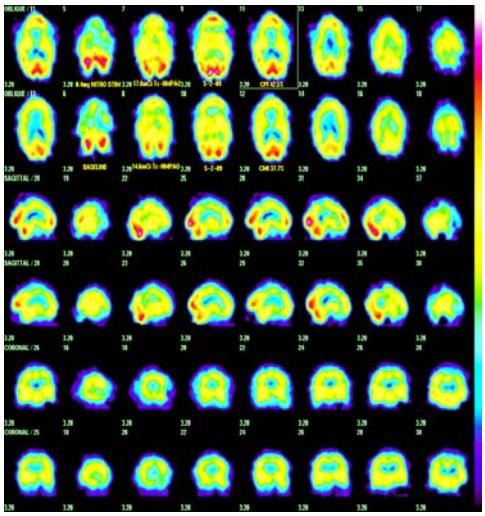
4. Below on the left is brain SPECT for a 53 year-old hyperlipidemic woman who had a TIA and thereafter an initial CMi 47.3%, CPi 37.8%, BMi 152%, BPi 88.4%; BMPi 171%, consistent with mainly vascular disease, who was treated with antiplatelet (clopidrogrel 75 mg qd) and statin (atorvastatin 80 mg or rosuvastatin 10 mg) therapy for one year. Follow-up brain SPECT is shown on the right below with CMi 60.1%, CPi 53.1%, BMi 107%, BPi 177%, BMPi 230%, when her TYM test was 50/50 (unusually good for an American!). We are hopeful that further improvement may ensue with cilostazol which was used as the perfusion stimulant in the second study and has consistently been similar in our experience to other cerebral perfusion stimulants.





5. Brain SPECT below on the left shows CMi 40.9%, CPi 31.8%, BMPi 156%, for an 84 year-old hyperlipidemic woman with memory loss and confusion, history of pituitary adenoma (1.8 cm), hyperprolactinemia, stage 3 renal failure (GFR 40 ml/min) and breast cancer in remission, who was treated with simvastatin 20 mg each evening, cabergoline 0.25 mg twice per week, clopidrogrel 75 mg qd, cilostazol 50 mg bid, l-thyroxine 25 to 50 mcg po qd, and namenda 10 mg bid for 7 months, after which brain SPECT, below on the right showed CMi 37.7%, CPi 42.5%, BMPi 218%, consistent with interval improvement. This patient shows remarkable reliability of the BMPi calculation, which predicted significant potential for recovery despite CPi < 33%, moderately severe dementia initially (MMSE 22/30) and the patient's advanced age of 84 years.





Summary

Calculation of the Brain Metabolic index (BMi) and Brain Perfusion index (BPi) and their cross product dependant Brain Metabolic-Perfusion index (BMPi) provide unique information about the potential for patients to respond to therapy for cognitive impairment. Normalization and scale factors may be further refined with more accurate volume averaging and more intuitive normalizations but are nonetheless remarkably reproducible, especially when comparing tracers of similar energy and using images with similar statistics and resolution.